

A<sup>1</sup>  
cont. impurities as determined by high pressure liquid chromatography (HPLC) and having a bacterial count of less than 250 ufc/ml and free of pathogens sufficient to form an acceptable pharmaceutical nasal spray dosage form. The solvent may be purified water suitable for use in nasal dosage forms or any equivalent water (e.g. injectable water) that is allowed for use in such nasal dosage forms. See REMINGTON'S PHARMACEUTICAL SCIENCES, any edition from 1980-1996. For the adequate and/or sufficient treatment and control of gastroparesis, a typical dose is that dose which is therapeutically effective and which minimizes side-effects and drug interactions.

✓  
Please replace the paragraph beginning at page 10, line 29, and ending at page 10, line 36, with the following:

A<sup>2</sup> Various techniques may be used to assess the severity of the gastroparesis and gastric emptying. Methods well known in this art include, for example, questioning the patient on symptoms related to the disease as well as techniques such as radiosciintigraphy, ultrasonography, and techniques using radiopaque markers such as barium. Radiosciintigraphy appears to be the preferred method, due to its relatively high sensitivity and specificity, ease of use, and low exposure to radiation. All of these methods can be used to determine, together with teachings of the present invention, the appropriate dosage for a particular patient.

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Please replace the paragraph beginning at page 11, line 1, and ending at page 11, line 8, with the following:

A<sup>3</sup> The weight of the patient may also affect the dosage to be administered. Typically, a dose of between about 0.1 mg/kg to about 2.5 mg/kg is given to a patient suffering from gastroparesis. The dosages can be either about 0.1 mg/kg, 0.2 mg/kg, 0.3 mg/kg, 0.4 mg/kg, 0.5 mg/kg, 0.6 mg/kg, 0.7 mg/kg, 0.8 mg/kg, 0.9 mg/kg, 1.0 mg/kg, 1.1 mg/kg, 1.2 mg/kg, 1.3 mg/kg, 1.4 mg/kg, 1.5 mg/kg, 1.6 mg/kg, 1.7 mg/kg, 1.8 mg/kg, 1.9 mg/kg, 2.0 mg/kg, 2.1 mg/kg, 2.2 mg/kg, 2.3 mg/kg, 2.4 mg/kg, 2.5 mg/kg. A preferred nasal dosage is between about 0.06 to about 1.2 mg/kg of body weight. Other preferred nasal dosages are about .06 mg/kg, .08 mg/kg, 1.0 mg/kg, 1.2 mg/kg and 1.4 mg/kg.

✓  
Please replace the paragraph beginning at page 11, line 10, and ending at page 11, line 33, with the following:

A4

The expected benefit of an intranasal formulation of metoclopramide for gastroparesis is to provide an alternative route of administration for this agent to patients who have uncomfortable gastrointestinal symptoms of gastroparesis. The intranasal formulation of metoclopramide will spare patients with active symptoms the potential additional discomfort of having to swallow an oral formulation and serves as an alternative to injectable formulations. As presented in greater detail below in Section 6, the nasal administration of metoclopramide treatment of gastroparesis offers many benefits, some of which are unexpected. For example, as illustrated below, one unexpected benefit is that while patents receiving the nasal form of the drug were exposed to less drug overall, 10 mg of nasal metoclopramide was superior to 10 mg oral metoclopramide in reducing symptoms with particular significance in the categories of feeling full after eating and persistent fullness. Further, less exposure to metoclopramide reduces the opportunity for central nervous system (CNS) side effects (*see* the data relating to  $AUC_{0-inf}$  for 10 mg oral versus nasal). Also, the benefit of the 20 mg nasal (80 mg/day) was superior than 10 mg oral in for all symptoms studied and was well tolerated for six weeks. In contrast, 80 mg/day of oral metoclopramide would be expected to result in significant CNS side effects and is not indicated for such duration. However, nasal doses of 80 mg/day were well tolerated for an extended period of six weeks. Further, because of its rapid onset of action (*see* Figures 2B and 2C showing higher initial blood levels, *i.e.*, faster absorption), nasal metoclopramide may be substituted for intravenous administration in patients with severe gastroparesis for whom the oral form is not indicated. The benefits of nasal administration over intravenous administration being obvious to the skilled practitioner. In sum, the nasal form of metoclopramide, as demonstrated herein, provides heretofore unexpected benefits in the treatment of gastroparesis.

**In the Claims:**

✓  
Please cancel Claims 1 – 20 without prejudice.